WHAT IS CLAIMED:

1. A method for identifying a mutant nucleic acid sequence differing by one or more single-base changes, insertions, or deletions, from a normal target nucleotide sequences, said method comprising:

providing a sample potentially containing the normal target nucleotide sequence as well as the mutant nucleic acid sequence;

providing two labeled oligonucleotide primers suitable for hybridization on complementary strands of the target nucleotide sequence and the mutant nucleic acid sequence;

providing a polymerase;

blending the sample, the labeled oligonucleotide primers, and the polymerase to form a polymerase chain reaction mixture;

subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a hybridization treatment, wherein oligonucleotide primers can hybridize to the target nucleotide sequence and/or the mutant nucleic acid sequence, an extension treatment, wherein the hybridized oligonucleotide primer is extended to form an extension product complementary to the target nucleotide sequence and/or the mutant nucleic acid sequence to which the oligonucleotide primer is hybridized, and a denaturation treatment, wherein hybridized nucleic acid sequences are separated;

inactivating the polymerase;

denaturing the polymerase chain reaction extension products;

annealing the polymerase chain reaction extension products to form heteroduplexed products potentially containing the normal target nucleotide sequence and the mutant nucleic acid sequence;

providing an endonuclease which preferentially nicks or cleaves heteroduplexed DNA at a location one base away from mismatched base pairs;

blending the heteroduplexed products and the endonuclease to form an endonuclease cleavage reaction mixture;

incubating the endonuclease cleavage reaction mixture so that the endonuclease preferentially nicks or cleaves heteroduplexed products at a location one base away from mismatched base pairs;

providing a ligase;

blending the potentially nicked or cleaved heteroduplexed products and the ligase to form a ligase resealing reaction mixture;

incubating the ligase resealing reaction mixture to seal the nicked heteroduplexed products at perfectly matched base pairs but with substantially no resealing of nicked heteroduplexed products at locations adjacent to mismatched base pairs;

separating products resulting from said incubating the ligase resealing reaction mixture by size or electrophoretic mobility; and

detecting the presence of the normal target nucleotide sequence and the mutant nucleic acid sequence in the sample by distinguishing the separated products resulting from said incubating the ligase resealing reaction mixture.

2. A method according to claim 1, wherein the target nucleotide sequence is genomic DNA.

3. A method according to claim 1, wherein the target nucleotide sequence is isolated from tumor samples.

4. A method according to claim 1, wherein the target nucleotide sequence is a double stranded cDNA copy of mRNA.

5. A method according to claim 1, wherein the target nucleotide sequence is a PCR amplified fragment.

6. A method according to claim 1, wherein the two labeled oligonucleotide primers are labeled with fluorescent dyes, IR dyes, or radioactive groups.

7. A method according to claim 6, wherein the two labeled oligonucleotide primers are labeled at their 5' ends.

8. A method according to claim 1, wherein the polymerase is either a native or recombinant thermostable polymerase from *Thermus aquaticus, Thermus thermophilus, Pyrococcus furiosus,* or *Thermotoga maritima.*

9. A method according to claim 1, wherein the polymerase chain reaction is initiated by adding either the polymerase or metal co-factors at temperatures above 65°C to the polymerase chain reaction mixture.

10. A method according to claim 1, wherein said denaturing the polymerase chain reaction extension products is carried out by heating to a temperature of 80-105°C.

11. A method according to claim 1, wherein said annealing the polymerase chain reaction extension products is carried out by cooling first to a temperature of 20-85°C and then to room temperature.

12. A method according to claim 1, wherein the endonuclease is Endonuclease V from *Thermotoga maritima.*

13. A method according to claim 1, wherein the endonuclease nicks or cleaves heteroduplexed products at a location 3' from mismatched base pairs.

14. A method according to claim 1, wherein said incubating the ligase resealing reaction mixture is carried out at a pH value between 7.2 and 7.8 when measured at 25°C.

15. A method according to claim 1, wherein the endonuclease cleavage reaction mixture further comprises $MgCl_2$ at a concentration of 2-7 mM.

16. A method according to claim 15, wherein the endonuclease to heteroduplexed product ratio in the endonuclease cleavage reaction mixture is in a range of 10:1 to 100:1.

17. A method according to claim 15, wherein the endonuclease cleavage reaction mixture contains substantially no NaCl or KCl.

18. A method according to claim 1, wherein the endonuclease cleavage reaction mixture further comprises $MnCl_2$ at a concentration of 0.4-1.2 mM.

19. A method according to claim 18, wherein the endonuclease to heteroduplexed product ratio in the endonuclease cleavage reaction mixture is in a range of 1:1 to 1:10.

20. A method according to claim 18, wherein the endonuclease cleavage reaction mixture comprises 50-100 mM NaCl or KCl.

21. A method according to claim 1, wherein the endonuclease cleavage reaction mixture contains DMSO in a range of 2.5 to 10 volume %.

22. A method according to claim 1, wherein the endonuclease cleavage reaction mixture contains betaine in a concentration of 0.5M to 1.5M.

23. A method according to claim 1, wherein said incubating the endonuclease cleavage reaction mixture is carried out at 50-65°C.

24. A method according to claim 1, wherein the ligase is a thermostable ligase.

25. A method according to claim 24, wherein the ligase is from *Thermus* species AK16D.

26. A method according to claim 24, wherein the ligase is from *Thermus aquaticus*, *Thermus thermophilus*, *Pyrococcus furiosus*, or *Thermotoga maritima*.

27. A method according to claim 24, wherein the ligase resealing reaction mixture contains 50-150 mM KCl to inhibit further endonucleolytic cleavage.

28. A method according to claim 1, wherein said separating is carried out by using denaturing polyacrylamide gel electrophoresis.

29. A method according to claim 1, wherein said separating is carried out by using capillary gel electrophoresis.

30. A method according to claim 1, wherein the ratio of the mutant nucleic acid sequence to the normal target nucleotide sequence is in a range of 1:20 to 20:1.

31. A method according to claim 1, wherein the polymerase chain reaction extension products have a length in the range of 50 bp to 1,700 bp.

32. A method according to claim 1, wherein the endonuclease preferentially cleaves mismatches within the heteroduplexed products selected from the group consisting of A/A, G/G, T/T, A/G, A/C, G/A, G/T, T/G, T/C, C/A, and C/T.

33. A method according to claim 1, wherein the endonuclease preferentially nicks or cleaves at least one of the heteroduplexed products formed for any single base mutation or polymorphism, except those having a sequence selected from the group consisting of gRcg, rcRc, cgYc and gYgy, where the position of the mismatch is underlined and shown in upper case.

34. A method according to claim 1, wherein the endonuclease preferentially nicks or cleaves one, two, and three base insertions or deletions within the heteroduplexed products.

35. A method according to claim 1, wherein said method distinguishes an inherited or sporadic mutation or polymorphism from a polymorphism in the normal target sequence.

36. A method according to claim 1, wherein the inherited or sporadic mutation or polymorphism is distinguished in a tumor suppressor gene, oncogene, or DNA replication or repair gene.

37. A method according to claim 38, wherein the gene is selected from the group consisting of Bcl2, Mdm2, Cdc25A, Cyclin D1, Cyclin E1, Cdk4, survivin, HSP27, HSP70, p53, $p21^{Cip}$, $p16^{Ink4a}$, $p19^{ARF}$, $p15^{INK4b}$, $p27^{Kip}$, Bax, growth factors, EGFR, Her2-neu, ErbB-3, ErbB-4, c-Met, c-Sea, Ron, c-Ret, NGFR, TrkB, TrkC, IGF1R, CSF1R, CSF2, c-Kit, AXL, Flt-1 (VEGFR-1), Flk-1 (VEGFR-2), PDGFRα, PDGFRβ, FGFR-1, FGFR-2, FGFR-3, FGFR-4, other protein tyrosine kinase receptors, β-catenin, Wnt(s), Akt, Tcf4, c-Myc, n-Myc, Wisp-1, Wisp-3, K-*ras*, H-*ras*, N-*ras*, c-Jun, c-Fos, PI3K, c-Src, Shc, Raf1, TGFβ, and MEK, E-Cadherin, APC, TβRII, Smad2, Smad4, Smad 7, PTEN, VHL, BRCA1, BRCA2, ATM, hMSH2, hMLH1, hPMS1, hPMS2, and hMSH3.

38. A method according to claim 1, wherein the endonuclease is a thermostable endonuclease which preferentially nicks or cleaves heteroduplexed DNA at a location where base pairs are mismatched or one base beyond the mismatch and generates ends which are suitable for ligation when nicking perfectly matched DNA.

39. A method according to claim 1, wherein the endonuclease is a thermostable endonuclease which preferentially nicks or cleaves heteroduplexed DNA at A/A, G/G, T/T, A/G, A/C, G/A, G/T, T/G, T/C, C/A, or C/T mismatched base pairs at a location where the base pairs are mismatched or one base beyond the mismatch

and generates ends which are suitable for ligation when nicking perfectly matched DNA.

40. A method according to claim 1, wherein the endonuclease is a thermostable endonuclease which preferentially nicks or cleaves at least one heteroduplex formed for any single base mutation or polymorphism, except those having gRcg, rcRc, cgYc, or gYgy sequences, where the position of the mismatch is underlined and shown in upper case, and generates ends which are suitable for ligation when nicking perfectly matched DNA.

41. A method according to claim 1, wherein the endonuclease is a thermostable endonuclease which preferentially nicks or cleaves heteroduplexed DNA containing one, two, and three base insertions or deletions, at a location where the base pairs are mismatched or one base beyond the unpaired bases, and generates ends which are suitable for ligation when nicking DNA at perfect matched DNA.

42. A method according to claim 1, wherein the endonuclease is a mutant endonuclease which preferentially nicks or cleaves at least one heteroduplexed DNA, containing mismatched bases, better than a wild-type endonuclease.

43. A method according to claim 42, wherein one of the mismatched bases in at least one of the heteroduplexed DNA is an "A".

44. A method according to claim 42, wherein one of the mismatched bases in at least one of the heteroduplexed DNA is a "G".

45. A method according to claim 1, wherein the endonuclease is a mutant endonuclease V from *Thermotoga maritima* containing either: (1) a Y80A residue change; (2) a Y80F residue change; (3) either a Y80L, Y80I, Y80V or Y80M residue change; (4) an R88A residue change; (5) an R88L, R88I, R88V, or R88M residue change; (6) an R88K residue change; (7) an R88N or R88Q residue change; (8) an R88D or R88E residue change; (9) an R88T or R88S residue change; (10) a

E89A residue change; (11) a E89L, E89I, E89V, or E89M residue change; (12) a E89D residue change; (13) a E89N or E89Q residue change; (14) a E89R or E89K residue change; (15) a E89T or E89S residue change; (16) a H116A residue change; (17) a H116L, H116I, H116V, or H116M residue change; (18) a H116K or H116R residue change; (19) a H116N or H116Q residue change; (20) a H116T or H116S residue change; (21) a K139A residue change; (22) a K139L, K139I, K139V, or K139M residue change; (23) a K139R residue change; (24) a K139N or K139Q residue change; (25) a K139D or K139E residue change; (26) a K139T or K139S residue change; (27) a D43A residue change; (28) a D43E residue change; (29) a D105A residue change; (30) a D105E residue change; (31) an F46A residue change; (32) an F46Y residue change; (33) an F46L, F46I, F46V, or F46M residue change; (34) an R118A residue change; (35) an R118L, R118I, R118V, or R118M residue change; (36) an R118K residue change; (37) an R118N or R118Q residue change; (38) an R118D or R118E residue change; (39) an R118T or R118S residue change; (40) a F180A residue change; (41) a F180Y residue change; (42) a F180L, F180I, F180V, or F180M residue change; (43) a G83A residue change; (44) a G83L, G83I, G83V, or G83M residue change; (45) a G83K or G83R residue change; (46) a G83N or G83Q residue change; (47) a G83D or G83E residue change; (48) a G83T or G83S residue change; (49) an I179A residue change; (50) an I179K or I179R residue change; (51) an I179N or I179Q residue change; (52) an I179D or I179E residue change; (53) an I179T or I179S residue change; (54) a D110A residue change; or (55) an H125A residue change.

46. A method for identifying a mutant nucleic sequence differing by one or more single-base changes, insertions, or deletions from a normal target nucleic acid sequence, said method comprising:

providing a sample potentially containing the mutant nucleic acid sequence but not necessarily the normal target nucleic acid sequence;

providing a standard containing the normal target nucleic acid sequence;

providing two labeled oligonucleotide primers suitable for hybridization on complementary strands of the mutant nucleic acid sequence;

providing a polymerase;

blending the sample, the standard, the labeled oligonucleotide primers, and the polymerase to form a first polymerase chain reaction mixture;

subjecting the first polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a hybridization treatment, wherein the labeled oligonucleotide primers can hybridize to the mutant nucleic acid sequence, an extension treatment, wherein the hybridized oligonucleotide primer is extended to form an extension product complementary to the mutant nucleic acid sequence to which the oligonucleotide primer is hybridized, and a denaturation treatment, wherein hybridized nucleic acid sequences are separated;

inactivating the polymerase;

providing the normal target nucleic acid sequence;

blending the normal target nucleic acid sequence, the labeled oligonucleotide primers, and the polymerase to form a second polymerase chain reaction mixture;

subjecting the second polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a hybridization treatment, wherein the labeled oligonucleotide primers can hybridize to the normal target nucleic acid sequence, an extension treatment, wherein the hybridized oligonucleotide primer is extended to form an extension product complementary to the normal target nucleic acid sequence to which the oligonucleotide primer is hybridized, and a denaturation treatment, wherein hybridized nucleic acid sequences are separated;

inactivating the polymerase;

blending the first and second polymerase chain reaction extension products;

denaturing the first and second polymerase chain reaction extension products;

annealing the first and second polymerase chain reaction extension products to form heteroduplexed products potentially containing the normal target nucleic acid sequence and the mutant nucleic acid sequence;

providing an endonuclease which preferentially nicks or cleaves heteroduplexed DNA at a location one base away from mismatched base pairs;

blending the heteroduplexed products and the endonuclease to form an endonuclease cleavage reaction mixture;

incubating the endonuclease cleavage reaction mixture so that the endonuclease preferentially nicks or cleaves heteroduplexed products at a location one base away from mismatched base pairs;

providing a ligase;

blending the potentially nicked or cleaved heteroduplexed products and the ligase to form a ligase resealing reaction mixture;

incubating the ligase resealing reaction mixture to seal the nicked heteroduplexed products at perfectly matched base pairs but with substantially no resealing of nicked heteroduplexed products at locations adjacent to mismatched base pairs;

separating products resulting from said incubating the ligase resealing reaction mixture by size or electrophoretic mobility; and

detecting the presence of the normal target nucleic acid sequence and the mutant nucleic acid sequence target nucleotide in the sample by distinguishing the separated products resulting from said incubating the ligase resealing reaction mixture.

47. A method according to claim 46, wherein the target nucleotide sequence is genomic DNA.

48. A method according to claim 46, wherein the target nucleotide sequence is isolated from tumor samples.

49. A method according to claim 46, wherein the target nucleotide sequence is a double stranded cDNA copy of mRNA.

50. A method according to claim 46, wherein the target nucleotide sequence is a PCR amplified fragment.

51. A method according to claim 46, wherein the two labeled oligonucleotide primers are labeled with fluorescent dyes, IR dyes, or radioactive groups.

52. A method according to claim 51, wherein the two labeled oligonucleotide primers are labeled at their 5' ends.

53. A method according to claim 46, wherein the polymerase is either a native or recombinant thermostable polymerase from *Thermus aquaticus, Thermus thermophilus, Pyrococcus furiosus,* or *Thermotoga maritima.*

54. A method according to claim 46, wherein the polymerase chain reaction is initiated by adding either the polymerase or metal co-factors at temperatures 65-94°C to the polymerase chain reaction mixture.

55. A method according to claim 46, wherein said denaturing the polymerase chain reaction extension products is carried out by heating to a temperature above 94°C.

56. A method according to claim 46, wherein said annealing the polymerase chain reaction extension products is carried out by cooling first to 50-85°C and then to room temperature.

57. A method according to claim 46, wherein the endonuclease is Endonuclease V from *Thermotoga maritima.*

58. A method according to claim 46, wherein the endonuclease nicks or cleaves heteroduplexed products at a location on the 3' side one base away from mismatched base pairs.

59. A method according to claim 46, wherein said incubating the ligase resealing reaction mixture is carried out at a pH value between 7.2 and 7.8 when measured at 25°C.

60. A method according to claim 46, wherein the endonuclease cleavage reaction mixture further comprises $MgCl_2$ at a concentration of 2-7 mM.

61. A method according to claim 60, wherein the endonuclease to heteroduplexed product ratio in the endonuclease cleavage reaction mixture is in a range of 10:1 to 100:1.

62. A method according to claim 60, wherein the endonuclease cleavage reaction mixture contains substantially no NaCl or KCl.

63. A method according to claim 46, wherein the endonuclease cleavage reaction mixture further comprises $MnCl_2$ at a concentration of 0.4-1.2 mM.

64. A method according to claim 63, wherein the endonuclease to heteroduplexed product ratio in the endonuclease cleavage reaction mixture is in a range of 1:1 to 1:10.

65. A method according to claim 63, wherein the endonuclease cleavage reaction mixture comprises 25-75 mM NaCl or KCl.

66. A method according to claim 46, wherein the endonuclease cleavage reaction mixture contains DMSO in a range of 2.5% to 10 volume %.

67. A method according to claim 46, wherein the endonuclease cleavage reaction mixture contains betaine in a concentration of 0.5M to 1.5M.

68. A method according to claim 46, wherein said incubating the endonuclease cleavage reaction mixture is carried out at 65°C for 1 hour.

69. A method according to claim 46, wherein the ligase is a thermostable ligase.

70. A method according to claim 69, wherein the ligase is from *Thermus* species AK16D.

71. A method according to claim 69, wherein the ligase is from *Thermus aquaticus*, *Thermus thermophilus*, *Pyrococcus furiosus*, or *Thermotoga maritima*.

72. A method according to claim 69, wherein the ligase resealing reaction mixture contains 25-75 mM KCl to inhibit further endonucleolytic cleavage.

73. A method according to claim 46, wherein said separating is carried out by using denaturing polyacrylamide gel electrophoresis.

74. A method according to claim 46, wherein said separating is carried out by using capillary gel electrophoresis.

75. A method according to claim 46, wherein the ratio of the mutant nucleic acid sequence to the normal target nucleotide sequence is in a range of 1:20 to 20:1.

76. A method according to claim 46, wherein the polymerase chain reaction extension products have a length in the range of 50 bp to 1,700 bp.

77. A method according to claim 46, wherein the endonuclease preferentially cleaves mismatches within the heteroduplexed products selected from the group consisting of A/A, G/G, T/T, A/G, A/C, G/A, G/T, T/G, T/C, C/A, and C/T.

78. A method according to claim 46, wherein the endonuclease preferentially nicks or cleaves at least one of the heteroduplexed products formed for any single base mutation or polymorphism, except those having a sequence selected from the group consisting of gRcg, rcRc, cgYc and gYgy, where the position of the mismatch is underlined and shown in upper case.

79. A method according to claim 46, wherein the endonuclease preferentially nicks or cleaves one, two, and three base insertions or deletions within the heteroduplexed products.

80. A method according to claim 46, wherein said method distinguishes an inherited or sporadic mutation or polymorphism from a polymorphism in the normal target sequence.

81. A method according to claim 46, wherein the inherited or sporadic mutation or polymorphism is distinguished in a tumor suppressor gene, oncogene, or DNA replication or repair gene.

82. A method according to claim 81, wherein the gene is selected from the group consisting of Bcl2, Mdm2, Cdc25A, Cyclin D1, Cyclin E1, Cdk4, survivin, HSP27, HSP70, p53, $p21^{Cip}$, $p16^{Ink4a}$, $p19^{ARF}$, $p15^{INK4b}$, $p27^{Kip}$, Bax, growth factors, EGFR, Her2-neu, ErbB-3, ErbB-4, c-Met, c-Sea, Ron, c-Ret, NGFR, TrkB, TrkC, IGF1R, CSF1R, CSF2, c-Kit, AXL, Flt-1 (VEGFR-1), Flk-1 (VEGFR-2), PDGFRα, PDGFRβ, FGFR-1, FGFR-2, FGFR-3, FGFR-4, other protein tyrosine kinase receptors, β-catenin, Wnt(s), Akt, Tcf4, c-Myc, n-Myc, Wisp-1, Wisp-3, K-*ras*, H-*ras*, N-*ras*, c-Jun, c-Fos, PI3K, c-Src, Shc, Raf1, TGFβ, and MEK, E-Cadherin, APC, TβRII, Smad2, Smad4, Smad 7, PTEN, VHL, BRCA1, BRCA2, ATM, hMSH2, hMLH1, hPMS1, hPMS2, and hMSH3.

83. A method according to claim 46, wherein the endonuclease is a thermostable endonuclease which preferentially nicks or cleaves heteroduplexed DNA

at a location where base pairs are mismatched or one base beyond the mismatch and generates ends which are suitable for ligation when nicking perfectly matched DNA.

84. A method according to claim 46, wherein the endonuclease is a thermostable endonuclease which preferentially nicks or cleaves heteroduplexed DNA at A/A, G/G, T/T, A/G, A/C, G/A, G/T, T/G, T/C, C/A, or C/T mismatched base pairs at a location where the base pairs are mismatched or one base beyond the mismatch and generates ends which are suitable for ligation when nicking perfectly matched DNA.

85. A method according to claim 46, wherein the endonuclease is a thermostable endonuclease which preferentially nicks or cleaves at least one heteroduplex formed for any single base mutation or polymorphism, except those having gRcg, rcRc, cgYc, or gYgy sequences, where the position of the mismatch is underlined and shown in upper case, and generates ends which are suitable for ligation when nicking perfectly matched DNA.

86. A method according to claim 46, wherein the endonuclease is a thermostable endonuclease which preferentially nicks or cleaves heteroduplexed DNA containing one, two, and three base insertions or deletions, at a location where the base pairs are mismatched or one base beyond the unpaired bases, and generates ends which are suitable for ligation when nicking DNA at perfect matched DNA.

87. A method according to claim 46, wherein the endonuclease is a mutant endonuclease which preferentially nicks or cleaves at least one heteroduplexed DNA, containing mismatched bases, better than a wild-type endonuclease.

88. A method according to claim 87, wherein one of the mismatched bases in at least one of the heteroduplexed DNA is an "A".

89. A method according to claim 87, wherein one of the mismatched bases in at least one of the heteroduplexed DNA is a "G".

90. A method according to claim 46, wherein the endonuclease is a mutant endonuclease V from *Thermotoga maritima* containing either: (1) a Y80A residue change; (2) a Y80F residue change; (3) either a Y80L, Y80I, Y80V or Y80M residue change; (4) an R88A residue change; (5) an R88L, R88I, R88V, or R88M residue change; (6) an R88K residue change; (7) an R88N or R88Q residue change; (8) an R88D or R88E residue change; (9) an R88T or R88S residue change; (10) a E89A residue change; (11) a E89L, E89I, E89V, or E89M residue change; (12) a E89D residue change; (13) a E89N or E89Q residue change; (14) a E89R or E89K residue change; (15) a E89T or E89S residue change; (16) a H116A residue change; (17) a H116L, H116I, H116V, or H116M residue change; (18) a H116K or H116R residue change; (19) a H116N or H116Q residue change; (20) a H116T or H116S residue change; (21) a K139A residue change; (22) a K139L, K139I, K139V, or K139M residue change; (23) a K139R residue change; (24) a K139N or K139Q residue change; (25) a K139D or K139E residue change; (26) a K139T or K139S residue change; (27) a D43A residue change; (28) a D43E residue change; (29) a D105A residue change; (30) a D105E residue change; (31) an F46A residue change; (32) an F46Y residue change; (33) an F46L, F46I, F46V, or F46M residue change; (34) an R118A residue change; (35) an R118L, R118I, R118V, or R118M residue change; (36) an R118K residue change; (37) an R118N or R118Q residue change; (38) an R118D or R118E residue change; (39) an R118T or R118S residue change; (40) a F180A residue change; (41) a F180Y residue change; (42) a F180L, F180I, F180V, or F180M residue change; (43) a G83A residue change; (44) a G83L, G83I, G83V, or G83M residue change; (45) a G83K or G83R residue change; (46) a G83N or G83Q residue change; (47) a G83D or G83E residue change; (48) a G83T or G83S residue change; (49) an I179A residue change; (50) an I179K or I179R residue change; (51) an I179N or I179Q residue change; (52) an I179D or I179E residue change; (53) an I179T or I179S residue change; (54) a D110A residue change; or (55) an H125A residue change.

91. A thermostable endonuclease which preferentially nicks or cleaves heteroduplexed DNA at a location where base pairs are mismatched or one

base beyond the mismatch and generates ends which are suitable for ligation when nicking perfectly matched DNA.

92. A thermostable endonuclease which preferentially nicks or cleaves heteroduplexed DNA at A/A, G/G, T/T, A/G, A/C, G/A, G/T, T/G, T/C, C/A, or C/T mismatched base pairs at a location where the base pairs are mismatched or one base beyond the mismatch and generates ends which are suitable for ligation when nicking perfectly matched DNA.

93. A thermostable endonuclease which preferentially nicks or cleaves at least one heteroduplex formed for any single base mutation or polymorphism, except those having gRcg, rcRc, cgYc, or gYgy sequences, where the position of the mismatch is underlined and shown in upper case, and generates ends which are suitable for ligation when nicking perfectly matched DNA.

94. A thermostable endonuclease which preferentially nicks or cleaves heteroduplexed DNA containing one, two, and three base insertions or deletions, at a location where the base pairs are mismatched or one base beyond the unpaired bases, and generates ends which are suitable for ligation when nicking DNA at perfect matched DNA.

95. A mutant endonuclease which preferentially nicks or cleaves at least one heteroduplexed DNA, containing mismatched bases, better than a wild-type endonuclease.

96. A mutant endonuclease according to claim 95, wherein one of the mismatched bases in at least one of the heteroduplexed DNA is an "A".

97. A mutant endonuclease according to claim 95, wherein one of the mismatched bases in at least one of the heteroduplexed DNA is a "G".

98. A mutant endonuclease V from *Thermotoga maritima* containing either: (1) a Y80A residue change; (2) a Y80F residue change; (3) either a Y80L, Y80I, Y80V or Y80M residue change; (4) an R88A residue change; (5) an R88L, R88I, R88V, or R88M residue change; (6) an R88K residue change; (7) an R88N or R88Q residue change; (8) an R88D or R88E residue change; (9) an R88T or R88S residue change; (10) a E89A residue change; (11) a E89L, E89I, E89V, or E89M residue change; (12) a E89D residue change; (13) a E89N or E89Q residue change; (14) a E89R or E89K residue change; (15) a E89T or E89S residue change; (16) a H116A residue change; (17) a H116L, H116I, H116V, or H116M residue change; (18) a H116K or H116R residue change; (19) a H116N or H116Q residue change; (20) a H116T or H116S residue change; (21) a K139A residue change; (22) a K139L, K139I, K139V, or K139M residue change; (23) a K139R residue change; (24) a K139N or K139Q residue change; (25) a K139D or K139E residue change; (26) a K139T or K139S residue change; (27) a D43A residue change; (28) a D43E residue change; (29) a D105A residue change; (30) a D105E residue change; (31) an F46A residue change; (32) an F46Y residue change; (33) an F46L, F46I, F46V, or F46M residue change; (34) an R118A residue change; (35) an R118L, R118I, R118V, or R118M residue change; (36) an R118K residue change; (37) an R118N or R118Q residue change; (38) an R118D or R118E residue change; (39) an R118T or R118S residue change; (40) a F180A residue change; (41) a F180Y residue change; (42) a F180L, F180I, F180V, or F180M residue change; (43) a G83A residue change; (44) a G83L, G83I, G83V, or G83M residue change; (45) a G83K or G83R residue change; (46) a G83N or G83Q residue change; (47) a G83D or G83E residue change; (48) a G83T or G83S residue change; (49) an I179A residue change; (50) an I179K or I179R residue change; (51) an I179N or I179Q residue change; (52) an I179D or I179E residue change; (53) an I179T or I179S residue change; (54) a D110A residue change; or (55) an H125A residue change.

99. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a Y80A residue change.

100. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a Y80F residue change.

101. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a Y80L, Y80I, Y80V or Y80M residue change.

102. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R88A residue change.

103. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R88L, R88I, R88V, or R88M residue change.

104. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R88K residue change.

105. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R88N or R88Q residue change.

106. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R88D or R88E residue change.

107. A mutant endonuclease V according to claim 98 wherein the endonuclease V contains an R88T or R88S residue change.

108. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an E89A residue change.

109. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an E89L, E89I, E89V, or E89M residue change.

110. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an E89D residue change.

111. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an E89N or E89Q residue change.

112. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an E89R or E89K residue change.

113. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an E89T or E89S residue change.

114. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a H116A residue change.

115. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a H116L, H116I, H116V, or H116M residue change.

116. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a H116K or H116R residue change.

117. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a H116N or H116Q residue change.

118. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a H116D or H116E residue change.

119. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a H116T or H116S residue change.

120. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a K139A residue change.

121. A mutant endonuclease V according to claim 98 wherein the endonuclease V contains a K139L, K139I, K139V, or K139M residue change.

122. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a K139R residue change.

123. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a K139N or K139Q residue change.

124. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a K139D or K139E residue change.

125. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a K139T or K139S residue change.

126. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a D43A residue change.

127. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a D43E residue change.

128. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a D105A residue change.

129. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a D105E residue change.

130. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an F46A residue change.

131. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an F46Y residue change.

132. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an F46L, F46I, F46V, or F46M residue change.

133. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R118A residue change.

134. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R118L, R118I, R118V, or R118M residue change.

135. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R118K residue change.

136. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R118N or R118Q residue change.

137. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R118D or R118E residue change.

138. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an R118T or R118S residue change.

139. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an F180A residue change.

140. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an F180Y residue change.

141. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an F180L, F180I, F180V, or F180M residue change.

142. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a G83A residue change.

143. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a G83L, G83I, G83V, or G83M residue change.

144. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a G83K or G83R residue change.

145. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a G83N or G83Q residue change.

146. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a G83D or G83E residue change.

147. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a G83T or G83S residue change.

148. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an I179A residue change.

149. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an I179K or I179R residue change.

150. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an I179N or I179Q residue change.

151. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an I179D or I179E residue change.

152. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an I179T or I179S residue change.

153. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains a D110A residue change.

154. A mutant endonuclease V according to claim 98, wherein the endonuclease V contains an H125A residue change.

155. A method for identifying a mutant nucleic acid sequence differing by one or more single-base changes, insertions, or deletions, from a normal target nucleic acid sequence, said method comprising:

providing a sample potentially containing the normal target nucleic acid sequence as well as the mutant nucleic acid sequence;

providing two labeled oligonucleotide primers suitable for hybridization on complementary strands of the target nucleic acid sequence and the mutant nucleic acid sequence;

providing a polymerase;

blending the sample, the labeled oligonucleotide primers, and the polymerase to form a polymerase chain reaction mixture;

subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a hybridization treatment, wherein oligonucleotide primers can hybridize to the target nucleic acid sequence and/or the mutant nucleic acid sequence, an extension treatment, wherein the hybridized oligonucleotide primer is extended to form an extension product complementary to the target nucleic acid sequence and/or the mutant nucleic acid sequence to which the oligonucleotide primer is hybridized, and a denaturation treatment, wherein hybridized nucleic acid sequences are separated;

inactivating the polymerase;

denaturing the polymerase chain reaction extension products;

annealing the polymerase chain reaction extension products to form heteroduplexed products potentially containing the normal target nucleic acid sequence and the mutant nucleic acid sequence;

providing an endonuclease which preferentially nicks or cleaves heteroduplexed DNA at a location one base away from mismatched base pairs;

blending the heteroduplexed products and the endonuclease to form an endonuclease cleavage reaction mixture;

incubating the endonuclease cleavage reaction mixture so that the endonuclease preferentially nicks or cleaves heteroduplexed products at a location one base away from mismatched base pairs;

providing a ligase;

blending the potentially nicked or cleaved heteroduplexed products and the ligase to form a ligase resealing reaction mixture;

incubating the ligase resealing reaction mixture to seal the nicked heteroduplexed products at perfectly matched base pairs but with substantially no resealing of nicked heteroduplexed products at locations adjacent to mismatched base pairs;

providing a polymerase with 3'-5' exonuclease activity;

blending the potentially nicked or cleaved heteroduplexed products and the polymerase with 3'-5' exonuclease activity to form a polymerase exonucleolytic degradation reaction mixture;

incubating the polymerase exonucleolytic degradation reaction mixture under conditions effective for the 3'-5' exonucleolytic activity to remove several bases 3' to the nick;

inactivating the polymerase with 3'-5' exonuclease activity:

providing a polymerase without 3'-5' activity;

blending the incubated polymerase degradation reaction mixture, the polymerase without 3'-5' activity, labeled dideoxyterminator triphosphate nucleotides, and deoxyribonucleotide triphsophates to form a polymerase mini-sequencing reaction mixture;

incubating the polymerase mini-sequencing reaction mixture under conditions effective for the polymerase without 3'-5' activity to extend the 3' end of the nicked or cleaved heteroduplexed products to form mini-sequencing reaction products;

separating the mini-sequencing products by size or electrophoretic mobility; and

detecting the presence of normal target nucleic acid sequence and the mutant nucleic acid sequence by distinguishing the separated mini-sequencing products resulting from said incubating the polymerase mini-sequencing reaction mixture.